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Original contribution

Ectopic primary intrathyroidal thymoma: a clinicopathological and immunohistochemical analysis of 3 cases☆

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Summary Thymomas are rare tumors that occasionally arise from ectopic locations. Ectopic thymomas originating within the thyroid gland are an exceedingly uncommon clinical entity that has only been described sporadically. In this study, we present the clinicopathological and immunohistochemical features of 3 primary intrathyroidal thymomas. The patients were 2 women and 1 man between the ages of 43 and 53 years (average, 48 years). Clinically, the patients presented with neck pain or enlarged thyroid glands. Physical examination and thyroid ultrasound revealed the presence of nodular masses confined to the thyroid parenchyma. No concurrent mediastinal tumors were identified in any of the cases, and none of the patients had a history of thymoma. Fine needle aspirate performed in 1 case was interpreted as possibly Hashimoto thyroiditis. Surgical resection was performed in all cases. Grossly, the lesions were circumscribed masses measuring from 1 to 4 cm in size. Histologically, the lesions showed the classic biphasic cellular proliferation of thymomas characterized by varying proportions of epithelial cells and lymphocytes. Two patients remain alive and well 1.5 to 2 years after their surgical resection, whereas the third patient was lost to follow-up. The cases herein presented highlight an unusual tumor entity that can be clinically confused for more common lesions affecting the thyroid gland. Awareness of this entity is important to avoid misdiagnosis and secure appropriate clinical management.

1. Introduction

Thymomas are epithelial tumors of the thymic gland that usually arise in the anterior superior mediastinum. These tumors are rare neoplasms comprising less than 1% of adult cancers [1]. Ectopic thymomas are thought to arise from aberrant thymic tissue displaced during embryologic development and are extremely rare, accounting for only up to 4% of all thymomas [2]. Reported sites of ectopic thymoma include the neck, posterior and middle mediastinum, trachea, pericardium, lung, and pleural cavity, their distribution and frequency reflecting those of ectopic thymic tissue [3-9]. Another uncommon primary site of such tumors is the thyroid gland. Previously, tumors reported as primary intrathyroidal thymomas (PITs) comprised a heterogeneous group of neoplasms that, in addition to true thymomas, included entities later redefined as "spindle epithelial tumor with thymus-like differentiation" (SETTLE) and "carcinoma showing thymus-like differentiation" (CASTLE) [10]. PITs

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also need to be separated from ectopic cervical thymomas that often occur in the general region of the thyroid near the thoracic inlet but are either separate from or only adhere to the inferior poles of the gland. Taking these facts into account, thymomas arising completely within the thyroid parenchyma are exceptionally uncommon, and to the best of our knowledge, only 5 previous cases have been reported in the medical literature [10-13].

Here, we report a series of 3 cases of these unusual tumors and describe their clinical, morphological, and immunohistochemical features. Awareness of this entity is not only important for diagnostic purposes but also for treatment planning and prognosis.

2. Materials and methods

Three cases of ectopic PIT were encountered in the files of the Department of Pathology at MD Anderson Cancer Center in Houston, TX, and the consultation files of 1 of the authors (C. A. M.). All available histologic material, which consisted of hematoxylin and eosin–stained sections from resection specimens, was reviewed. Unstained slides for immunohistochemical studies were available in 1 of the cases. Tissue sections were incubated with antibodies against pancytokeratin (1:100; Dako, Carpinteria, CA), cytokeratin (CK) 5/6 (1:50; Dako), thyroid transcription factor 1 [TTF-1] (1:200; Dako), Pax8 (1:100; ProteinTech Group, Chicago, IL), and terminal deoxynucleotidyl transferase (TdT) (1:50; Dako). Adequate positive and negative controls were run, respectively. Clinical information was obtained by reviewing the respective clinical charts or by contacting the referring physicians. The study was approved by the institutional review board.

3. Results

3.1. Clinical findings

The clinical features of our cases are summarized in the Table. The patients were 2 females and 1 male with an age range from 43 to 53 years (mean, 48 years). The main presenting symptoms included neck pain, palpable neck nodule, or enlargement of the thyroid gland but no symptoms to suggest hypothyroidism or hyperthyroidism. In addition, signs or symptoms of autoimmune disease were absent, and thyroid function tests were within normal limits in all cases. Physical examination and thyroid ultrasound revealed the presence of nodular masses confined to the thyroid parenchyma. No concurrent mediastinal lesions were identified in any of the cases, and none of the patients had a prior history of a primary mediastinal tumor. Two of the lesions were situated in the left thyroid lobe; and 1, in the right. Fine needle aspiration (FNA) was performed in 1 patient and was interpreted as possible Hashimoto thyroiditis. Surgical resection in the form of hemithyroidectomy or subtotal thyroidectomy was performed in all cases. Clinical follow-up revealed that 2 patients were alive and well 1.5 to 2 years after their surgical resection, whereas the third patient was lost to follow-up.

3.2. Gross findings

The tumors were well-circumscribed firm lesions contained within the thyroid parenchyma ranging in size from 1 to 4 cm in maximum dimension. The tumors were pale tan in color and had a homogenous cut surface. Delicate fibrous bands traversing the tumors could be identified in all cases. Areas of hemorrhage or necrosis were not identified. A rim

Table Clinicopathological features of primary intrathyroidal thymomas

Case	Reference	Sex	Age (y)	Clinical features	Tumor site	Gross features	Treatment	Outcome
1	Lewis et al 1987 [12]	F	40	NK	Right lobe	Circumscribed; 2.5 cm	Surgical resection	A&W at 7 y
2	Asa et al 1988 [11]	M	35	Thyroid mass	Right lobe	Invasive; size NK	Surgical resection; adjuvant radiotherapy	A&W at 16 y (after 2 recurrences)
3	Chan and Rosai 1991 [10]	F	71	Neck mass	Left lobe	Invasive; 6.5 cm	Surgical resection	NK
4	Chan and Rosai 1991 [10]	F	38	Neck mass	Isthmus	Encapsulated; 6.4 cm	Surgical resection	NK
5	Cohen et al 2003 [13]	F	39	Enlarged thyroid	Left lobe	Encapsulated; 7.3 cm	Surgical resection	A&W at 3 y
6	New case	M	48	Neck pain, enlarged thyroid	Left lobe	Circumscribed; 4.0 cm	Surgical resection	A&W at 1.5 y
7	New case	F	53	Thyroid nodule	Left lobe	Circumscribed; 1.0 cm	Surgical resection	A&W at 2 y
8	New case	F	43	Enlarged thyroid	Right lobe	Circumscribed; 3.5 cm	Surgical resection	NK

Abbreviations: F, female; M, male; NK, not known; A&W, alive and well.